NOV 2 8 2008

Attachment 1

This report is required by law (? USC 21 43) Failure to report according to the regulations can result in an order to cease and desist and to be subject lo penalties as provided for in Section 2150

Set reverse side for additionalinformation

Interagency Report Control No 0180-DOA-AN

UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

1. REGISTRATION NO. 52-R-0007 #493

FORM APPROVED
OMB NO. 0579-0036

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA include Zip Code)

Virginia Commonwealth University
Division of Animal Resources, Box 980630
Richmond, VA 23298-0630

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITYLOCATIONS (Sites)

See attached sheet

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS FORM 7023A)

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain-relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used	E. Number of animals upon which teaching experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. *(An explanation of the procedures producing pain or distress in those animals and the reasons such drugs were not used must be attached to this report)*	F. TOTAL NO OF ANIMALS (Cols. C + D + E)
4. Dogs			67		67
5. Cats			7		7
6. Guinea Pigs			80		80
7. Hamsters			12		12
8. Rabbits			449	15	464
9. Non-human Primates	3	17	37	16	70
10. Sheep			11		11
11., Pigs			223		223
12. Other Farm Animals					
Chickens		16			16
13 Other Animals					
Ferrets		4	86		90
Frogs		35	10		45

ASSURANCE STATEMENTS

1) Professionally acceptable standards governing the care, treatment, and use of animals including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility

2) Each principal investigator has considered alternatives to painful procedures.

3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). A summary of **all such exceptions is attached lo this annual report.** In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.

4) The attending veterinarianfor this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(Chief Executive Officer or Legally Responsible Institutional Official)
I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

SIGNATURE OF CEO OR INSTITUTIONAL OFFICIAL	NAME & TITLE OF CEO OR INSTITUTIONAL OFFICIAL *(Type or Print)*	DATE SIGNED
(b)(6), (b)(7)c		11/26/08

APHIS FORM 7023 (Replaces VS FORM 18-23 (OCT 88) which is obsolete
(AUG 91)

Column E Explanation

This form is intended as an aid to completing the Column E explanation. It is not an official form and its use is voluntary. Names, addresses, protocols, veterinary care programs, and the like, are not required as part of an explanation. A Column E explanation must be written so as to be understood by lay persons as well as scientists.

1. Registration Number: 52-R-0007

2. Number of animals used in this study: 16

3. Species (common name) of animals used in the study: rhesus monkeys

4. Explain the procedure producing pain and/or distress.

   Sixteen rhesus monkeys were used as part of our program to evaluate drug dependence liability of new compounds. These rhesus monkeys are physically dependent on morphine. Periodically, they are allowed to go into spontaneous withdrawal, or withdrawal is precipitated by opioid antagonists. During this time they experience moderate to severe stress. Once in withdrawal, the monkeys are injected with the investigational compound, or morphine, or saline and then observed to assess their withdrawal state. On completion of the observation period, all withdrawal signs and symptoms are relieved by an injection of morphine. It is important to note that while these experiments are repetitive in nature, a new investigational chemical is being tested on each occasion. Many of these chemicals are opioid in nature and relieve the withdrawal signs and symptoms.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with the test results. (For Federally mandated testing, see Item 6 below).

   The distress produced by this procedure is the end-point being measured. As indicated above, many of the compounds tested relieve these symptoms and the experiment is terminated immediately after the observation period by the administration of morphine which also relieves the withdrawal signs.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102)

   The results from our testing are used by both the FDA and the DEA in making decisions concerning the Controlled Substances Act.

1. Registration Number: 52-R-0007

2. Number of animals used in this study: 15

3. Species (common name) of animals used in the study: rabbits

4. Explain the procedure producing pain and/or distress.

Under sterile conditions, 16 anesthetized animals receive a balloon occluder placed around a major branch of the left coronary artery coursing on the anterior LV wall. The occluder tubing is tunneled under the skin, and exteriorized through a small incision between the scapulae. The rabbits are allowed to recover for a minimum of 7 days after surgery.

One week after the initial surgery, the rabbits consciously undergo a sequence of six 4-minute coronary occlusions interspersed with 4 minutes of reperfusion or administration of a pharmacological preconditioning drug prior to sustained ischemia for 30 min. The performance of successful coronary occlusions will be verified by observing the development of ST-segment elevation and changes in the QRS complex on the ECG and a drop in arterial blood pressure monitored from the ear dorsal artery. After ischemia, rabbits are allowed 72 hrs for recovery before their hearts are harvested for analysis of infarct size and protein expression.

In the event of development of ventricular fibrillation during ischemia in the conscious state, the rabbits are closely monitored along with their ECG recording for 10 min. If they do not return to normal sinus rhythm spontaneously (since no other possible intervention is available to defibrillate rabbits), the animals are sacrificed according to the protocol.

Before the induction of ischemia, the conscious rabbits will receive valium (4 mg/kg; IM) to minimize discomfort caused by the brief intermittent episodes of ischemia followed by sustained prolonged ischemia for 30 or 45 minutes. Since many patients may suffer ischemic period that could exceed 30 minutes, it is felt it is important to demonstrate that the pharmacological therapies are effective under more severe experimental conditions in the rabbit model. It is believed that extending the duration of ischemia up to 45 minutes does not cause additional stress or pain in these animals. Collaborators at another institution have recently performed 10 conscious rabbits with 45 minutes of occlusion period and observed no distress and no difference from 30 min of occlusion period.

Rabbits were chosen for this work as their cardiovascular system more closely models that of humans than mice and rats and this increases the translational quality of the study.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with the test results. (For Federally mandated testing, see Item 6 below).

The use of opiate analgesics such as morphine is avoided due to its preconditioning effects in the heart, which were well documented in rats (Schultz et al. Circ. Res. 78: 1100-1104, 1996) and rabbits (Miki et al. Mol. Cell. Biochem. 186: 3-12, 1998; Okubo et al. Am. J. Physiol. 287: H1786-H1791, 2004). Similar confounding effects may also be

caused by non-steroidal anti-inflammatory agent (NSAID), since a number studies showed infarct size-reducing effects of ibuprofen in dogs (Romson et al. Circulation 66: 1002-1011, 1982), cats (Flynn et al. Inflammation 8: 33-44, 1984) and rats (Gross et al. J. Pharmacol. Exp. Ther. 310: 185-191, 2004). Furthermore, the objective of this conscious model is to simulate a 'real-life' episode of heart attack where patients are not uniformly administered with analgesics or NSAIDs prior to a heart attack. For these reasons, the procedure uses only a high dose of valium which causes muscle relaxation, decreases anxiety and discomfort in the animals.

6. What, if any, federal regulations require this procedure? Cite the agency, the code of Federal Regulations (CFR) title number and the specific section number (e.g. APHIS, 9 CFR 113.102)

Not applicable.

Description of Exceptions to Applicable Regulations

- The IACUC has approved one exception as pertains to cage size. It has allowed a cage height of 30" to 31.5" (cages taper from front to back) for rhesus monkeys up to 15 kg in weight. The "Guide" recommends a cage height of 32". The design of the cage overcompensates on the floor space area at 9 square ft for one animal rather than the 6 square feet recommended.

- The IACUC has approved a protocol conducting surgical procedures on ferrets in an individual laboratory. VCU's Office of Environmental Health and Safety (OEHS) advised that the safety concerns regarding the injection of a replication incompetent recombinant herpes simplex virus into brain tissue outweighed the use of a dedicated surgical facility for this small animal, and the IACUC approved the use of a biosafety cabinet with the appropriate air flow.